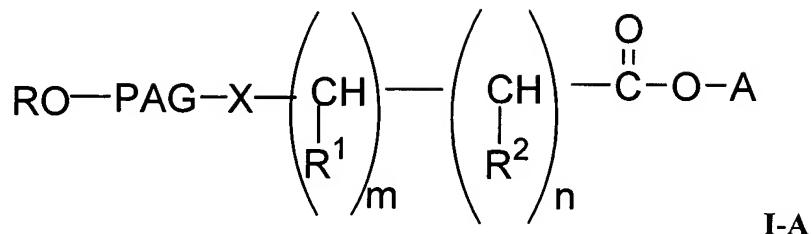


WHAT IS CLAIMED IS:

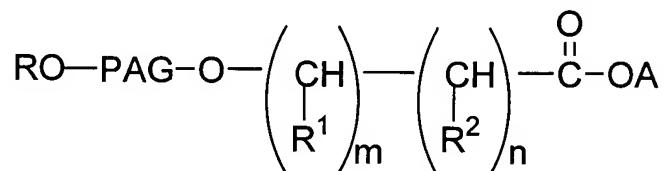
1. A compound of the formula



wherein R, R₁ and R₂ are individually hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons ; n is an integer of from 0 to 1; m is an integer of from 4 to 8; and A is a hydrogen or an activated leaving group which when taken together with its attached oxygen atom forms an ester

or hydrolyzable esters thereof wherein A is hydrogen.

2. The compound of claim 1 having the formula



I-A1

wherein A, R, PAG, R¹, R² m and n are as above.

3. The compound of claim 2 wherein A is hydrogen.

4. The compound of claim 3 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

5. The compound of claim 4 wherein R is methyl.

6. The compound of claim 5 wherein n is 0 and m is 4.

7. The compound of claim 5 wherein PEG has a molecular weight of from 10,000 to 40,000.

8. The compound of claim 6 wherein PEG has a molecular weight of from 20,000 to about 35,000.

9. The compound of claim 2 wherein A is an activated leaving group.

10. The compound of claim 9 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

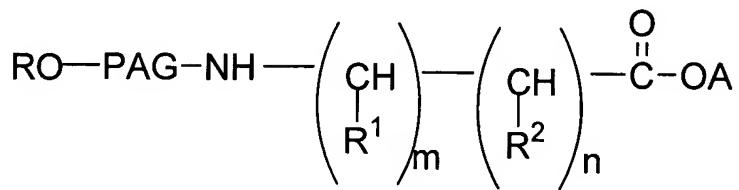
11. The compound of claim 9 wherein R is methyl.

12. The compound of claim 11 wherein n is 0 and m is 4.

13. The compound of claim 12 wherein PEG has a molecular weight of from 10,000 to 40,000.

14. The compound of claim 13 wherein PEG has a molecular weight of from 20,000 to about 35,000.

15. The compound of claim 1 wherein said compound has the formula



I-A2

wherein A, R, PAG, R¹, R², m and n are as above.

16. The compound of claim 15 wherein A is hydrogen.

17. The compound of claim 16 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

18. The compound of claim 17 wherein R is methyl.

19. The compound of claim 18 wherein n is 0 and m is 4.

20. The compound of claim 19 wherein PEG has a molecular weight of from 10,000 to 40,000.

21. The compound of claim 20 wherein PEG has a molecular weight of from 20,000 to about 35,000.

22. The compound of claim 18 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

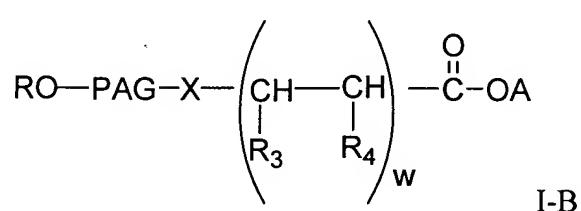
23. The compound of claim 22 wherein R is methyl.

24. The compound of claim 23 wherein n is 0 and m is 4.

25. The compound of claim 24 wherein PEG has a molecular weight of from 10,000 to 40,000.

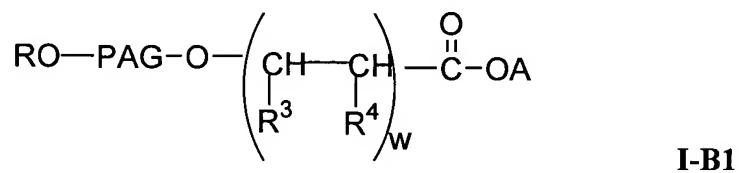
26. The compound of claim 25 wherein PEG has a molecular weight of from 20,000 to about 35,000.

27. The compound of formula



wherein R is hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons ; w is an integer of from 1 to 3; and one of R₃ and R₄ is lower alkyl and the other is hydrogen or lower alkyl; and A is a hydrogen or an activated leaving group which when taken together with its attached oxygen forms an ester, or hydrolyzable esters thereof wherein A is hydrogen.

28. The compound of claim 27 wherein said compound is



wherein A, R, PAG, R³, R⁴, w and n are as above.

29. The compound of claim 28 wherein A is hydrogen.

30. The compound of claim 29 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

31. The compound of claim 30 wherein R is methyl.

32. The compound of claim 31 wherein w is 1.

33. The compound of claim 32 wherein PEG has a molecular weight of from 10,000 to 40,000.

34. The compound of claim 33 wherein PEG has a molecular weight of from 20,000 to about 35,000.

35. The compound of claim 28 wherein A is an activated leaving group.

36. The compound of claim 35 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

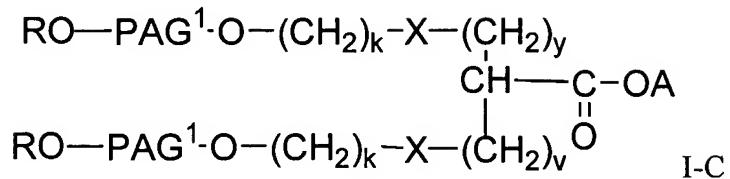
37. The compound of claim 36 wherein R is methyl.

38. The compound of claim 37 wherein w is 1.

39. The compound of claim 38 wherein PEG has a molecular weight of from 10,000 to 40,000.

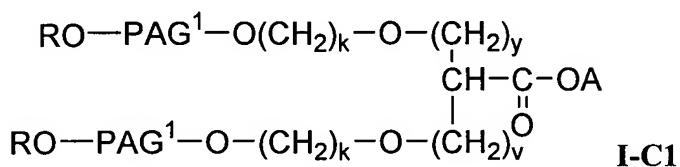
40. The compound of claim 39 wherein PEG has a molecular weight of from 20,000 to about 35,000.

41. The compound of formula



wherein R is hydrogen or lower alkyl, X is -O- or -NH-, A is a hydrogen or an activated leaving group which when taken together with its attached oxygen atom forms an ester, PAG¹ is a divalent residue of a polyalkylene glycol resulting from the removal of both of the terminal hydroxy groups, said residue having a molecular weight of from about 500 to about 25,000 Daltons, y is an integer from 0 to 3 and v is an integer from 1 to 3; and k is an integer from 1 to 2; or hydrolyzable esters thereof wherein A is hydrogen.

42. The compound of claim 41 wherein said compound has the formula



wherein R, PAG¹, A v, y and k are all as above.

43. The compound of claim 42 wherein A is hydrogen.

44. The compound of claim 43 wherein PAG¹ is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

45. The compound of claim 42 wherein each PAG¹ residue has a molecular weight of 500 to 15,000.

46. The compound of claim 42 wherein A is a leaving group.

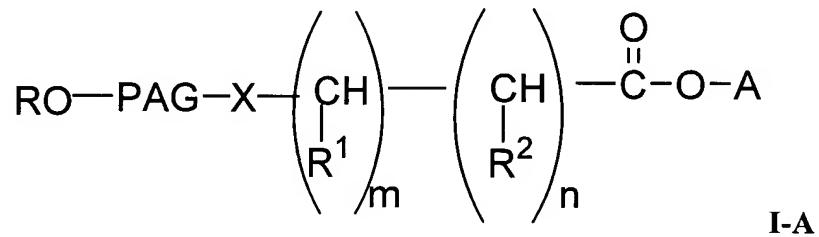
47. The compound of claim 46 wherein said leaving group is N-hydroxysuccinimidyl.

48. The compound of claim 47 wherein PAG¹ is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

49. The compound of claim 48 wherein R is methyl.

50. The compound of claim 49 wherein each PEG residue has a molecular weight of from 500 to 10,000.

51. A process for producing an activated ester of the formula:



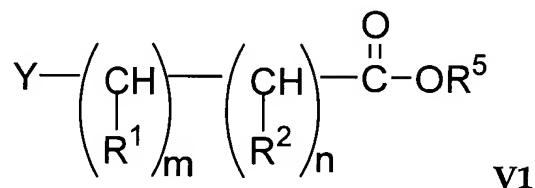
wherein R, R₁ and R₂ are individually hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons; n is an integer of from 0 to 1; m is an integer of from 4 to 8; and A is a

hydrogen or an activated leaving group which when taken together with its attached oxygen atom forms an ester comprising, condensing a compound of the formula:

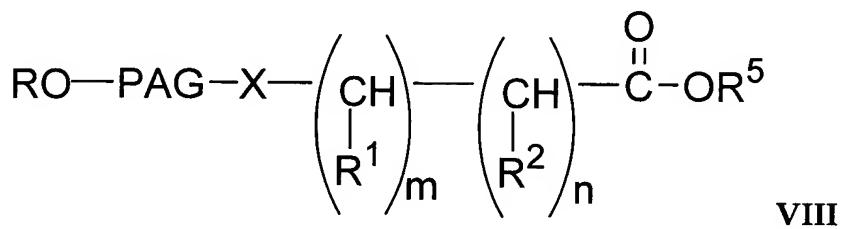


V

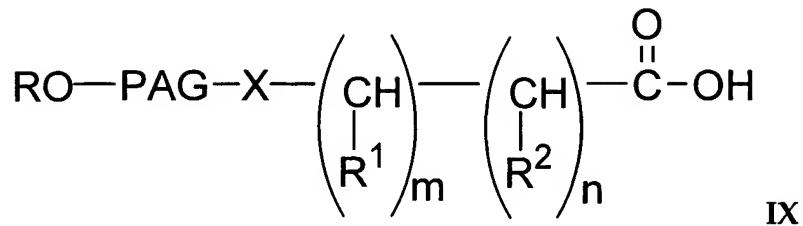
wherein R, and PAG are as above, and V is $-\text{OH}$ or $-\text{NH}_2$, with the compound of the formula:



wherein R^5 forms a hydrolyzable ester protecting group and Y is halide and R^1 , R^2 , m , and n , are as above, to produce an ester of the formula



wherein R, PAG, X, R^1 , R^2 , R^5 , m and n are as above, hydrolyzing said ester to form a free acid of the formula:

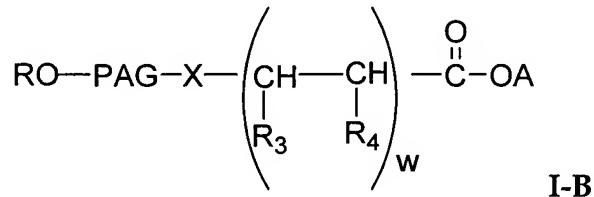


wherein R, PAG, X, R¹, R², m and n are as above,

and reacting said free acid with a halide of an activated leaving group in the presence of a coupling agent to produce said activated ester.

52. The process of claim 51 wherein said leaving group is N-hydroxysuccinimidyl group 58.

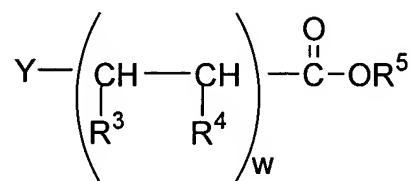
53. A process for producing an activated ester of the formula:



wherein R is hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkyleneglycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons; w is an integer of from 1 to 3; and one of R₃ and R₄ is lower alkyl and the other is hydrogen or lower alkyl; and A is a hydrogen or an activated

leaving group which when taken together with its attached oxygen atom forms an ester

comprising, condensing a compound of the formula:



XX

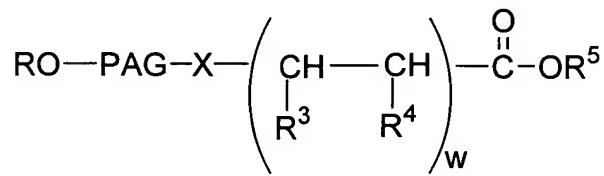
wherein w, Y, R³, R⁴ and R⁵ are as above, Y is halide and R⁵ forms a hydrolyzable protecting group

with a compound of the formula:



V

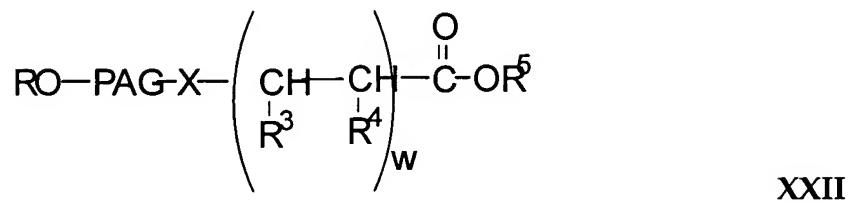
wherein R, and PAG are as above, V is -OH or -NH₂, to produce an ester of the formula:



XXI

wherein w, R, PAG, X, R³, R⁴ and R⁵ are as above

hydrolyzing said ester to form a free acid of the formula:

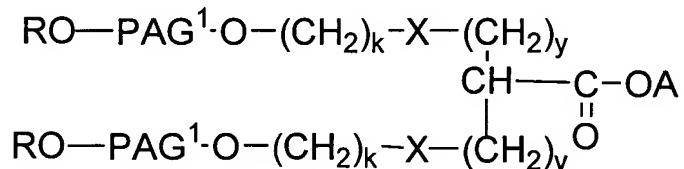


wherein R, PAG, X, R³, R⁴ and R⁵ are as above,

and reacting said free acid with a halide of an activated leaving group in the presence of a coupling agent to produce said activated ester.

54. The process of claim 53 wherein said leaving group is a N-hydroxysuccinimidyl group.

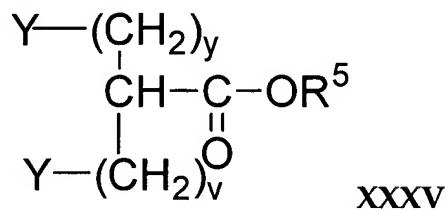
55. A process for producing an activated ester of the formula:



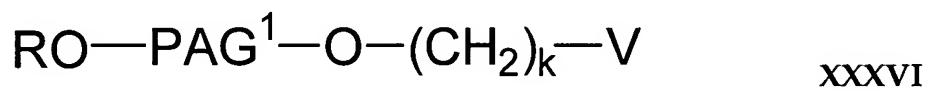
I-C

wherein R is hydrogen or lower alkyl, X is -O- or -NH, A is a hydrogen or an activated leaving group which when taken together with its attached oxygen atom forms an ester, PAG¹ is a divalent residue of a polyalkylene glycol resulting from the removal of both of the terminal hydroxy groups, said residue having a molecular weight of from about 500

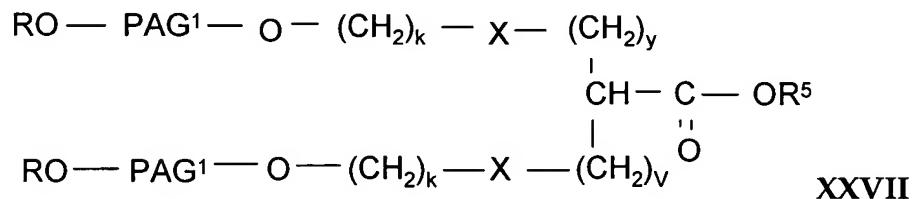
to about 25,000 Daltons, y is an integer from 0 to 3 and v is an integer from 1 to 3; and k is an integer from 1 to 2,
comprising, condensing a compound of the formula:



wherein Y is halide, y and v are as above, and R⁵ forms a hydrolyzable ester protecting group
with a compound of the formula

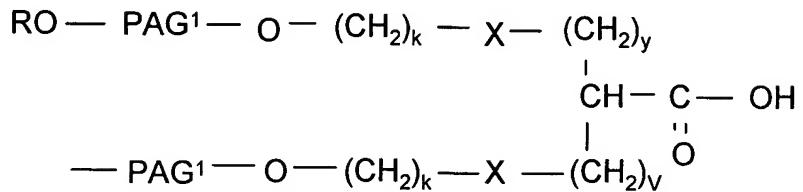


wherein R, PAG¹ and k are as above, V is -OH or -NH₂,
to produce an ester of the formula:



wherein R, PAG¹, X, R⁵, k, v and y are as above,

hydrolyzing said ester to form a free acid of the formula:



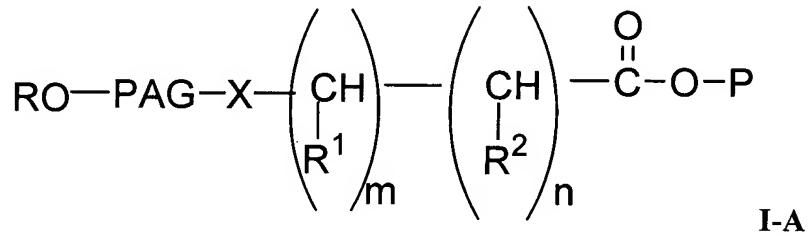
XXVIII

wherein R, PAG¹, X, k, v and y are as above,

and reacting said free acid with a halide of an activated leaving group in the presence of a coupling agent to produce said activated ester.

56. The process of claim 55 wherein said leaving group is N-hydroxysuccinimidyl.

57. A conjugate of the formula



wherein P is a residue of a biopharmaceutical having a terminal hydroxy group wherein the terminal hydroxy group is removed, R, R₁ and R₂ are individually hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a

molecular weight of from 1,000 to 50,000 Daltons; n is an integer of from 0 to 1; and m is an integer of from 4 to 8.

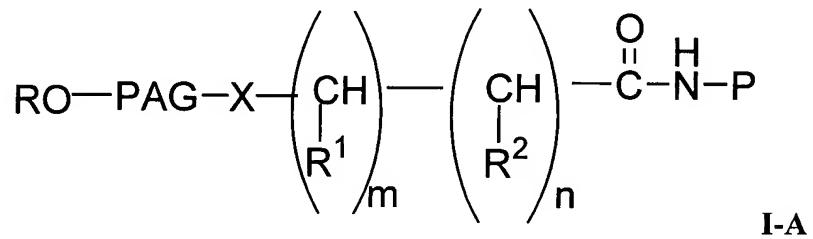
58. The conjugate of claim 57 wherein P is a glycoside.

59. The conjugate of claim 58 wherein P is a residue of AZT.

60. The conjugate of claim 57 wherein X is -0-.

61. The conjugate of claim 60 wherein PAG is a polyethylene glycol residue having a molecular weight of 10,000 to 15,000.

62. A conjugate of the formula



wherein P is a residue of a biopharmaceutical having a terminal hydroxy group wherein the terminal hydroxy group is removed, R, R₁ and R₂ are individually hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons; n is an integer of from 0 to 1; and m is an integer of from 4 to 8.

63. The conjugate of claim 62 wherein P is a residue of a protein or polypeptide.

64. The conjugate of claim 63 wherein X is -0-.

65. The conjugate of claim 64 wherein PAG is a polyethylene glycol residue having a molecular weight of about 10,000 to 15,000.

66. The conjugate of claim 63 wherein P is the polypeptide T-20 having a sequence according to SEQ ID NO: 1.

67. The conjugate of claim 64 wherein R is methyl.